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Application and Progress of Computational Fluid Dynamics in the Study and Treatment of Intracranial Aneurysms

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ABSTRACT. *With the advancement of imaging detection methods, the detection rate of intracranial aneurysms is increasing year by year. At the same time, the compressive cerebral neuropathy caused by the aneurysm itself and the brain injury caused by ruptured hemorrhage seriously affect the quality of life of patients.Because of the special blood flow pattern in aneurysms, hemodynamics has been a research hotspot in the field of aneurysms. At present, there is still no consensus on the study of hemodynamics in the occurrence, development and rupture mechanism of intracranial aneurysms.In this paper, the research progress of hemodynamic parameters such as shear force, blood flow pattern, computational fluid dynamics in intracranial aneurysms is summarized in combination with relevant literatures in recent years.*

KEYWORDS: *Intracranial Aneurysm; Hemodynamics; Shear Force; Computational Fluid Dynamics*

1. Introduction

Intracranial aneurysms are cystic bulges caused by local intracranial vascular lesions, with a population prevalence of about 3%[1,2]. And with the advancement of imaging technology and the increase of population health examination, the cases of screening aneurysms are increasing year by year.Rupture of intracranial aneurysm is also the main cause of non-traumatic subarachnoid hemorrhage. Once ruptured, it will cause a high mortality rate, and nearly half of the surviving patients will remain disabled [3-6], causing a huge burden to the patients themselves and society.Studies have shown that hemodynamics plays an important role in the occurrence, development and rupture of intracranial aneurysms, and has been verified by preliminary clinical studies [7,8].At present, the rapid development of computational fluid dynamics (CFD) provides a new means for the study of aneurysm hemodynamics. With the help of CFD method, the influence of the shear force of aneurysm wall, the form of blood flow on the occurrence, development and rupture of intracranial aneurysms can be studied.This article combines the relevant literature in recent years, and summarizes the above aspects.

2. Application of CFD in the Study of Intracranial Aneurysms

CFD is a kind of subject to simulate the flow, blood flow and other fluids by means of calculation. Its main research content is to solve the governing equation of fluid mechanics, namely Navier Stokes equation, by mathematical method. With the help of CFD technology, we can directly reconstruct human brain blood vessels and simulate the blood flow of aneurysms at different positions in vivo, so as to meet the clinical needs. At present, CFD technology has gradually matured, and the clinical operation process is also becoming more and more simple: mainly through MRA, CTA or DSA and other imaging means to obtain the three-dimensional data of the blood vessels, and then the reconstructed vessels are gridded, and the results are obtained by using software for finite element analysis.

At present, some achievements have been made in the study of intracranial aneurysms related to CFD. For example, the relationship between the morphology of intracranial aneurysms and their growth and rupture can be studied by means of CFD. Xiang et al. [9, 10] made morphological statistical analysis on 119 cases of ruptured and unruptured intracranial aneurysms, and concluded that the ratio of aneurysm length to parent artery radius in ruptured and unruptured aneurysms was statistically significant. In addition, new clinical techniques and new treatment methods can also be combined with CFD, such as CFD and 4D flow MRI technology can be combined to study the influence of tumor blood flow pattern on intracranial aneurysm. For new treatment methods, such as flow diverter (FD), CFD can also be used to evaluate the therapeutic effect after implantation, and the use of CFD technology to reconstruct blood vessels and blood flow can also be used to construct preoperative visualization model for complex intracranial aneurysms requiring bypass surgery, so as to improve the success rate of surgery. In a word, the application scope of CFD is mainly divided into two categories: one is to explore the relationship between shear force and the progression and rupture of intracranial aneurysms by calculating shear force; the other is to explore the relationship between blood flow pattern and the progression and rupture of intracranial aneurysms through blood flow simulation.

3. Technical Problems of CFD Method

At present, although CFD has been widely used in clinical practice, there are many technical defects in this research method which can not be overcome. Firstly, in order to facilitate the calculation, the blood should be assumed as Newtonian fluid; secondly, the inherent elasticity of the vascular wall should be ignored in the calculation process. These idealized treatments will obviously lead to inaccurate

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calculation results. In addition, the existing CFD technology can not measure the tumor wall thickness in vivo, which affects the analysis effect of CFD on the condition of patients with intracranial aneurysm. In the clinical practice of using FD device to treat intracranial aneurysms, even if the best placement position of the mesh stent is simulated in the computer, the problem of incorrect placement will still appear in the actual operation [11], which is closely related to the technical defects of CFD.

At present, CFD simulation still needs a lot of manpower and time, and the calculation program is complicated and difficult to master. Although it has been initially applied in clinical practice, it is still only used as a research tool rather than a diagnostic tool [12-14]. The study of CFD in predicting the risk of ruptured intracranial aneurysms is also in its infancy and needs to be developed. In the future, the development of CFD should be combined with the biological indicators of intracranial aneurysms to improve the prediction effect of aneurysm rupture and other related risk factors. In addition to trying to overcome their own technical defects and make the simulation results more convincing, scholars at home and abroad should also unify the CFD standards as soon as possible, so that the CFD data of different research centers can exchange and integrate with each other, and even build a CFD big data platform for intracranial aneurysms, so that the future CFD research will develop towards a more convincing large sample research direction.

4. Relationship between Shear Stress and Progression and Rupture of Intracranial Aneurysms

The blood flow in the blood vessel mainly exerts three kinds of biological forces on the tube wall, which are shear force, pressure and mechanical tension. Among them, shear force directly acts on endothelial cells on the surface of lumen. Abnormal shear stress can cause a series of biological reactions of endothelial cells, which is considered as the main factor to promote the occurrence and development of intracranial aneurysms. With the development of CFD technology, the shear forces in different parts of the pipe wall can be calculated. Scholars have different opinions on the specific effects of shear stress on aneurysms. After studying 106 cases of middle cerebral artery aneurysms, Miura et al. [15-17] considered that low shear stress was the main factor leading to aneurysm rupture.

However, after the CFD statistical analysis of 210 cases of intracranial aneurysms, Cebral et al. [18] drew the opposite conclusion: the rupture of intracranial aneurysms is more likely to occur in the high shear zone with high concentration of jet. The inconsistent results also confirmed the complexity of the mechanism of intracranial aneurysms, that is, different types of shear stress may play different roles in the occurrence, development and rupture of intracranial aneurysms. Secondly, there is no uniform standard for the study of hemodynamics of intracranial aneurysms, and its technical defects may lead to inconsistent results.

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In addition, the diversity of research results of intracranial aneurysms is also reflected in the study of morphology and histology [19]. According to observation, kadasi et al. [19] classified intracranial aneurysms into three types according to their morphology: ① aneurysms with inner diameter less than 4 mm, thin, transparent and smooth, and mainly decellularized in histology; ② aneurysms with inner diameter greater than 10 mm, with irregular wall surface and mainly formed by atherosclerotic plaque in histology; ③ morphology between them. Similar results were obtained from histological analysis of intracranial aneurysms: small aneurysms have a higher probability (48%) of forming thin and transparent tumor walls, and the number of vascular smooth muscle cells and inflammatory cells in the tumor wall is less; the probability of thickening the aneurysm wall of large aneurysms is high, and most of them are accompanied by proliferation of vascular smooth muscle cells and inflammatory cells [20, 21].

Based on the above findings and the controversial results about the role of shear force on intracranial aneurysms, it is not difficult to see that the research on shear force and the mechanism of intracranial aneurysm progression and rupture should abandon single conclusion, and fully consider the complexity and diversity of intracranial aneurysm itself, and the research on the mechanism of shear force and intracranial aneurysm development and rupture should be abandoned In order to explore the internal mechanism of aneurysms, the effects of different types of shear stress obtained by CFD were further studied.

The potential impact of high shear stress on intracranial aneurysms clinical observation found that intracranial aneurysms mostly occurred at the bifurcation, which may be related to the strong impact of blood flow on the carina of the bifurcation. The results of CFD study also showed that the shear strength and gradient were high. The study on the end of basilar artery by Metaxa et al. [22-24] further confirmed that high shear force and high gradient shear force can induce the formation of intracranial aneurysm. The histological analysis of early intracranial aneurysms showed that a large number of proteases, mainly matrix metalloproteinase-2 and matrix metalloproteinase-9, were secreted by parietal cells in the early stage of intracranial aneurysms; However, inflammatory cell infiltration is not obvious in the early stage of intracranial aneurysms. The results show that high shear stress may have anti-inflammatory effect, which may be related to the early induction of intracranial aneurysms, and can induce a series of pathological changes in tumor wall cells.

The potential impact of low shear stress on intracranial aneurysms after the formation of early intracranial aneurysms, most of the intracranial aneurysms may have a trend of further enlargement, which will lead to the changes of hemodynamics in the aneurysms, and most of them are low shear stress and high shear shear index. Different studies have shown that low shear stress is mostly related to inflammation and atherosclerosis [7]. The specific manifestations of aneurysm wall under low shear stress environment are: endothelial cell loose, inflammatory cell infiltration, Macrophage Secretion of a large number of protease, vascular smooth muscle cell proliferation, cell phenotype changes and thrombosis

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[25-27]. Among them, inflammatory cell infiltration is particularly significant. It is suggested that the low shear stress environment may be conducive to the growth of inflammatory cells and the expansion of intracranial aneurysms. Moreover, the pro-inflammatory effect of low shear stress may be related to the further development of intracranial aneurysms.

Therefore, the difference of blood flow shear force can lead to anti-inflammatory or pro-inflammatory reaction of intracranial aneurysm wall, and then affect the stability of intracranial aneurysm wall. To determine the degree and trend of inflammation of intracranial aneurysms is of great significance for the prediction of the progression and rupture risk of intracranial aneurysms, and it is also of great significance to formulate the treatment indications for a large number of unruptured intracranial aneurysms.

5. Summary and Prospect

With the increasing detection rate of intracranial aneurysms in recent years, how to treat them effectively and reasonably is very important. The study of hemodynamics has a strong guiding significance for the diagnosis and treatment of intracranial aneurysms. At present, the study of hemodynamics of intracranial aneurysms mainly relies on various imaging methods. Although this kind of research is helpful to the diagnosis and treatment of intracranial aneurysms, it is important to find the relationship between mechanical effects and biological effects, which is divorced from the molecular biological mechanism of intracranial aneurysms. However, the research in this field is very difficult, and there is no mature animal model of hemodynamics to be used for research, and the related in vitro experiments are too divorced from the in vivo environment, so the research on hemodynamics of intracranial aneurysms is always unable to combine with the basic research. Although some related studies have been preliminarily recognized, the specific role of hemodynamics in the induction, progression and rupture of intracranial aneurysms is still unknown. The future research should focus on these technical problems, constantly improve the research on the mechanism of intracranial aneurysm, and combine the latest imaging methods and data simulation technology to push the research of intracranial aneurysm to a new height.

References

[1] Ravindra VM, de Havenon A, Gooldy TC, et al. Validation of the unruptured intracranial aneurysm treatment score: comparison with real-world cerebrovascular practice[J]. J Neurosurg, 2018, 129: 100-106
[2] Feng X, Qian Z, Zhang B, et al. Number of Cigarettes Smoked Per Day, Smoking Index, and Intracranial Aneurysm Rupture: A Case-Control Study[J]. Front Neurol, 2018, 9: 380
[3] Kaminogo M, Yonekura M, Shibata S. Incidence and outcome of multiple intracranial aneurysms in a defined population [J]. Stroke, 2003, 34: 16-21

ISSN 2706-6827 Vol. 2, Issue 8: 74-80, DOI: 10.25236/IJFS.2020.020810

[4] Seibert B, Tummala RP, Chow R, et al. Intracranial aneurysms: review of current treatment options and outcomes[J]. Front Neurol, 2011, 2: 45
[5] Wiebers DO, Whisnant JP, Huston JR, et al. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment[J], Lancet, 2003, 362: 103-110
[6] Nieuwkamp DJ, Setz LE, Algra A, et al. Changes in case fatality of aneurysmal subarachnoid haemorrhage over time, according to age, sex, and region: a meta-analysis[J]. Lancet Neurol, 2009, 8: 635-642
[7] Nixon AM, Gunel M, Sumpio BE. The critical role of hemodynamics in the development of cerebral vascular disease[J]. J Neurosurg, 2010, 112: 1240-1253
[8] Xiang J, Natarajan SK, Tremmel M, et al. Hemodynamicmorphologic discriminants for intracranial aneurysm rupture[J]. Stroke, 2011, 42: 144-152
[9] Walcott BP, Reinshagen C, Stapleton CJ, et al. Predictive modeling and in vivo assessment of cerebral blood flow in the management of complex cerebral aneurysms[J]. J Cereb Blood Flow Metab, 2016, 36: 998-1003
[10] Karmonik C, Diaz O, Klucznik R, et al. Quantitative comparison of hemodynamic parameters from steady and transient CFD simulations in cerebral aneurysms with focus on the aneurysm ostium[J]. J Neurointerv Surg, 2015, 7: 367-372
[11] Fr sen J. Flow Dynamics of Aneurysm Growth and Rupture: Challenges for the Development of Computational Flow Dynamics as a Diagnostic Tool to Detect Rupture-Prone Aneurysms[J]. Acta Neurochir Suppl, 2016, 123: 89-95
[12] Wong GK, Poon WS. Current status of computational fluid dynamics for cerebral aneurysms: the clinician's perspective[J]. J Clin Neurosci, 2011, 18: 1285-1288
[13] Baek H, Jayaraman MV, Richardson PD, et al. Flow instability and wall shear stress variation in intracranial aneurysms[J]. J RSoc Interface, 2010, 7: 967-988
[14] Miura Y, Ishida F, Umeda Y, et al. Low wall shear stress is independently associated with the rupture status of middle cerebral artery aneurysms[J]. Stroke, 2013, 44: 519-521
[15] Cebral JR, Mut F, Weir J, et al. Quantitative characterization of the hemodynamic environment in ruptured and unruptured brain aneurysms[J]. AJNR Am J Neuroradiol, 2011, 32: 145-151
[16] Kadasi LM, Dent WC, Malek AM. Cerebral aneurysm wall thickness analysis using intraoperative microscopy: effect of size and gender on thin translucent regions[J]. J Neurointerv Surg, 2013, 5: 201-206
[17] Kataoka K, Taneda M, Asai T, et al. Structural fragility and inflammatory response of ruptured cerebral aneurysms. A comparative study between ruptured and unruptured cerebral aneurysms[J]. Stroke, 1999, 30: 1396-1401
[18] Kataoka K, Taneda M, Asai T, et al. Difference in nature of ruptured and unruptured cerebral aneurysms[J]. Lancet, 2000, 355: 203
[19] Metaxa E, Tremmel M, Natarajan SK, et al. Characterization of critical hemodynamics contributing to aneurysmal remodeling at the basilar terminus in a rabbit model[J]. Stroke, 2010, 41: 1774-1782

ISSN 2706-6827 Vol. 2, Issue 8: 74-80, DOI: 10.25236/IJFS.2020.020810

[20] Kolega J, Gao L, Mandelbaum M, et al. Cellular and molecular responses of the basilar terminus to hemodynamics during intracranial aneurysm initiation in a rabbit model[J]. J Vasc Res, 2011, 48: 429-442

[21] Meng H, Tutino VM, Xiang J, et al. High WSS or Low WSS Complex interactions of hemodynamics with intracranial aneurysm initiation， growth， and rupture: toward a unifying hypothesis[J]. AJNR Am J Neuroradiol, 2014, 35: 1254-1262

[22] Galis ZS, Sukhova GK, Lark MW, et al. Increased expression of matrix metalloproteinases and matrix degrading activity in vulnerable regions of human atherosclerotic plaques[J]. J Clin Invest, 1994, 94: 2493-2503

[23] Chiu JJ, Chien S. Effects of disturbed flow on vascular endothelium: pathophysiological basis and clinical perspectives[J]. Physiol Rev, 2011, 91: 327-387

[24] Ross R. Atherosclerosis-an inflammatory disease[J]. N Engl J Med, 1999, 340: 115-126

[25] Mandelbaum M, Kolega J, Dolan JM, et al. A critical role for proinflammatory behavior of smooth muscle cells in hemodynamic initiation of intracranial aneurysm [J]. PLoS One, 2013, 8:e74357.

[26] Sforza DM, Kono K, Tateshima S, et al. Hemodynamics in growing and stable cerebral aneurysms[J]. J Neurointerv Surg, 2016, 8: 407-412

[27] Zhang Y, Hao J, Zheng Y, et al. Role of Kruppel-like factors in cancer stem cell[J]. J Physiol Biochem, 2015, 71: 155-164